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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/844,336	04/18/1997	PAMELA R. CONTAG	8678-004-999	7227

7590 04/16/2007

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EXAMINER	
ZEMAN, ROBERT A	

ART UNIT	PAPER NUMBER
1645	

MAIL DATE	DELIVERY MODE
04/16/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action Before the Filing of an Appeal Brief	**Application No.** 08/844,336	**Applicant(s)** CONTAG ET AL.	
	Examiner Robert A. Zeman	**Art Unit** 1645	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 14 March 2007 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☐ The period for reply expires _____months from the mailing date of the final rejection.
   b) ☒ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: *25 and 26*.
   Claim(s) rejected: *1-9,21 and 27*.
   Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: see attached.
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08) Paper No(s). _____
13. ☐ Other: _____.

ADVISORY ACTION

Applicant's response filed on 3-14-2007 is acknowledged. Claims 1, 3-9, 21-22 and 25-27 are pending.

Claim Rejections Maintained

35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The rejection of claims 1, 3-9 21, 22 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Menzel et al. (U.S. Patent 5,521,066) in view of Georgiou et al. (U.S. Patent 5,348,867 – IDS filed on 1-22-99) is maintained for reasons of record.

Applicant argues:

1. The pending claims require that the transducer be separate from the intracellular domain.

2. Menzel lacks the claimed transducer component entirely.

3. There is no motive to substitute Georgiou's scFv antibodies for Menzel's dimerization domain or ligand binding domain, because such substitutions would destroy the intended function of Menzel's system.

4. The rejection is based on improper hindsight reconstruction.

Applicant's arguments have been fully considered and deemed non-persuasive.

The instant claims are drawn to a biodetector comprising a transmembrane fusion protein comprising an extracellular ligand-specific moiety comprising an antibody and an intracellular enzymatic signal-transforming domain (i.e. signal-converting element); a transducer and a responsive element (transcription activation element) optionally coupled to a reporter gene (luciferase) via said responsive element. Said biodetector may further comprise a bacterial cell.

In response to applicant's argument that the references fail to show certain features of applicant's invention (Point 1), it is noted that the features upon which applicant relies (i.e., the transducer be separate from the intracellular domain) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

With regard to Point 2, the instant claims merely require a component that changes from an inactive to an active form in response to ligand binding and that that "change" activates a responsive element resulting in a detectable signal. As Menzel discloses the cytoplasmic domain of the wildtype or toxR fusion protein induces binding (via a conformational change) to the

promoter region (i.e. the transcription activation element) of the reporter gene (resulting in the expression of the reporter gene) in response to ligand binding to the ligand-binding domain of said fusion protein, the disclosure of Menzel meets the requirements of the instant claims with regard to the transducer.

In response to applicant's argument that there is no suggestion to combine the references (Point 3), the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, Menzel discloses that "a variety of ligand-binding domains" could be used (see column 2, lines 15-16). Moreover, contrary Applicant's assertion, the use of antibodies would not render Menzel's system inoperative. Menzel discloses that the "dimerization domain" (i.e. ligand binding domain) can be anything capable of forming a dimer (see column 4, lines32-36). Since certain antibody classes (e.g. IgA) can form dimmers they meet the requirements set forth by Menzel.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning (Point 4), it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the

applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

As outlined previously, Menzel et al. disclose host cells a transmembrane fusion protein comprising a ligand binding domain, a cytoplasmic toxR DNA binding region, a hydrophobic ToxR transmembrane region and a reporter gene operatively linked to the ctx operon (see column 1, line 65 to column 2, line 6). Menzel et al. further disclose that when a ligand binds to the ligand binding domain, the cytoplasmic domain of the fusion protein to undergo a conformational change which induces binding to the promoter region of the reporter gene (see column 2, lines 35-44). Finally, Menzel et al. disclose that their fusion protein can be used to generate signal using a variety of ligand-binding domains (see column 2, lines 15-16) and that any reporter gene known in the art can be used with the disclosed fusion protein (see column 4, lines 38-42) and that the disclosed fusion proteins can be expressed in bacterial hosts (see column 7, lines 7-8).

Menzel et al. differs from the claimed invention in that they do not explicitly disclose the use of the antibodies or derivatives thereof or the specific use of luciferase as the reporter.

Georgiou et al. disclose methods for the recombinant expression of heterologous proteins on the surface of bacteria (see abstract) including the expression of scFv (see column 6, lines 25-26).

Since Menzel et al. disclose that a variety of ligand binding domains can be used in their transmembrane fusion protein, it would have been obvious to one of skill in the art to use the heterologous scFv disclosed by Georgiou et al. in order to take advantage of the increase in

specificity, diversity and ease of production associated with the resulting fusion protein (biodetector).

Conclusion

Claims 1, 3-9, 21-22 and 27 are rejected.

Claims 25-26 are objected to for being dependent on a rejected claim.

Claims 25-26 are free of the art of record.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert A. Zeman whose telephone number is (571) 272-0866. The examiner can normally be reached on Monday- Thursday, 7am -5:30 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on (571) 272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov.

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ROBERT A. ZEMAN
PRIMARY EXAMINER

April 9, 2007